AMENDMENT TO THE CLAIMS

150. (Currently amended) A method of treating a subject with a B-cell malignancy <u>that expresses CD22 antigen</u>, the method comprising administering to the subject a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate, wherein the anti-CD22 antibody of the monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate comprises a light chain variable region having a sequence set forth in SEQ ID NO:19 and a heavy chain variable region having a sequence set forth in SEQ ID NO:27.

151. (Previously presented) The method of claim 150, wherein the anti-CD22 antibody is selected from a group consisting of a monoclonal antibody, a chimeric antibody, a human antibody, a humanized antibody, a single chain antibody, and a biologically active antibody fragment wherein the biologically active fragment is a Fab, a modified Fab, Fab', F(ab')2 or Fv, or a heavy chain monomer or dimer.

152. (Previously presented) The method of claim 151, wherein the anti-CD22 antibody is a humanized antibody.

153. (Previously presented) The method of claim 152, wherein the humanized antibody comprises a variable domain comprising human acceptor framework regions and non-human donor CDRs.

154. (Currently amended) The method of claim 153, wherein the ~~human acceptor framework regions of the variable domain of the heavy chain of the antibody are based on SEQ ID NOS:21 and 22 and comprise donor residues at positions 1, 28, 48, 72 and 97 in SEQ ID NO:8~~ <u>heavy chain variable region is further modified to include one or more backmutations and comprises a framework residue selected from one or more of positions 1, 28, 48, 72, and 97 (linear numbering) occupied by Glu, Arg, Ile, Ala, and Thr, respectively, wherein the remainder of the heavy chain framework region is occupied by residues of the human acceptor framework of SEQ ID NO: 27</u>.

155. (Currently amended) The method of claim 154, wherein the ~~antibody further comprises donor residues at positions 68 and 70 in SEQ ID NO:8~~ <u>heavy chain variable region is further</u>

modified to include one or more backmutations and comprises a framework residue selected from one or more of positions 68 and 70 (linear numbering) occupied by Ala and Leu, respectively.

156.   (Currently amended) The method of claim 152, wherein the ~~anti-CD22 antibody comprises a variable domain of the light chain comprising a human acceptor framework region based on SEQ ID NOS:17 and 18 and further comprising donor residues at positions 2, 4, 42, 43, 50 and 65~~ light chain variable region is further modified to include one or more backmutations and comprises a framework residue selected from one or more of positions 2, 4, 42, 43, 50, and 65 (linear numbering) occupied by Val, Val, Leu, His, Gln, and Asp, respectively, wherein the remainder of the light chain framework region is occupied by residues of the human acceptor framework of SEQ ID NO: 19.

157.   (Currently amended) The method of claim 156, wherein the ~~anti-CD22 antibody further comprises a donor residue at position 3 in SEQ ID NO:7~~ light chain variable region is further modified to include one or more backmutations and comprises a framework residue at position 3 (linear numbering) occupied by Val..

158.   (Previously presented) The method of claim 150, wherein the cytotoxic drug is calicheamicin.

159.   (Previously presented) The method of claim 158, wherein the calicheamicin is gamma calicheamicin or N-acetyl gamma calicheamicin.

160.   (Previously presented) The method of claim 158, wherein the calicheamicin derivative is functionalized with 3-mercapto-3-methyl butanoyl hydrazide.

161.   (Previously presented) The method of claim 150, wherein the therapeutically effective dose of the composition is administered subcutaneously, intraperitoneally, intravenously, intraarterially, intramedullarly, intrathecally, transdermally, transcutaneously, intranasally, topically, enterally, intravaginally, sublingually or rectally.

162.   (Previously presented) The method of claim 161, wherein the therapeutically effective dose of the composition is administered intravenously.

163.   (Previously presented) The method of claim 150, wherein the subject is a human subject.

164.   (Previously presented) The method of claim 150, wherein the B-cell malignancy is a leukemia, a lymphoma or a Non-Hodgkin's lymphoma.

165-166. (Canceled)

167.   (Previously presented) The method of claim 150, comprising administering the therapeutically effective dose of the composition with one or more bioactive agents.

168.   (Previously presented) The method of claim 167, wherein the one or more bioactive agents are antibodies.

169.   (Previously presented) The method of claim 168, wherein the antibody is directed against a cell surface antigen expressed on B-cell malignancies.

170.   (Previously presented) The method of claim 169, wherein the antibody directed against cell surface antigens expressed on B-cell malignancies is selected from a group consisting of anti-CD19, anti-CD20 and anti-CD33 antibodies.

171.   (Previously presented) The method of claim 170, wherein the anti-CD20 antibody is rituximab.

172.   (Previously presented) The method of claim 168, wherein the therapeutically effective dose of the composition is administered together with an antibody directed against a cell surface antigen on B-cell malignancies, and optionally comprising one or more combinations of cytotoxic agents as a part of a treatment regimen, wherein the combination of cytotoxic agents is selected from:

   A. CHOPP (cyclophosphamide, doxorubicin, vincristine, prednisone, and procarbazine);

   B. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone);

   C. COP (cyclophosphamide, vincristine, and prednisone);

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D. CAP-BOP (cyclophosphamide, doxorubicin, procarbazine, bleomycin, vincristine, and prednisone);

E. m-BACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine, dexamethasone, and leucovorin);

F. ProMACE-MOPP (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, mechloethamine, vincristine, prednisone, and procarbazine);

G. ProMACE-CytaBOM (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, cytarabine, bleomycin, and vincristine);

H. MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, fixed dose prednisone, bleomycin, and leucovorin);

I. MOPP (mechloethamine, vincristine, prednisone, and procarbazine);

J. ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

K. MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABV (adriamycin/doxorubicin, bleomycin, and vinblastine);

L. MOPP(mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

M. ChlVPP (chlorambucil, vinblastine, procarbazine, and prednisone);

N. IMVP-16 (ifosfamide, methotrexate, and etoposide);

O. MIME (methyl-gag, ifosfamide, methotrexate, and etoposide);

P. DHAP (dexamethasone, high-dose cytarabine and cisplatin);

Q. ESHAP (etoposide, methylpredisolone, high-dose cytarabine, and cisplatin);

R. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

S. CAMP (lomustine, mitoxantrone, cytarabine, and prednisone);

T. CVP-1 (cyclophosphamide, vincristine, and prednisone). ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

U. ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

V. EPOCH (etoposide, vincristine, and doxorubicin for 96 hours with bolus doses of cyclophosphamide and oral prednisone);

W. ICE (ifosfamide, cyclophosphamide, and etoposide);

X. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

Y. CHOP-B. (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin); and

Z. P/DOCE (epirubicin or doxorubicin, vincristine, cyclophosphamide, and prednisone).

173. (Currently amended) A method of treating a subject with a B-cell malignancy that expresses CD22 antigen, the method comprising administering to the subject a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate, wherein the anti-CD22 antibody of the monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate comprises a light chain ~~variable region~~ having a sequence set forth in SEQ ID NO:28 and a heavy chain ~~variable region~~ having a sequence set forth in SEQ ID NO:30.

174. (Currently amended) The method of claim 173, wherein the anti-CD22 antibody is ~~selected from a group consisting of a monoclonal antibody, a chimeric antibody, a human antibody, a humanized antibody, a single chain antibody, and~~ a biologically active antibody fragment wherein the biologically active fragment is a Fab, a modified Fab, Fab', F(ab')2 or Fv, or a heavy chain monomer or dimer.

175-176. (Canceled)

177. (Currently amended) The method of claim ~~176~~ 173, wherein the ~~human acceptor framework regions of the variable domain of the heavy chain of the antibody are based on SEQ~~

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ID NOS:21 and 22 and comprise donor residues at positions 1, 28, 48, 72 and 97 in SEQ ID NO:8 heavy chain variable region is further modified to include one or more backmutations and comprises a framework residue selected from one or more of positions 1, 28, 48, 72, and 97 (linear numbering) occupied by Glu, Arg, Ile, Ala, and Thr, respectively, wherein the remainder of the heavy chain framework region is occupied by residues of the human acceptor framework of SEQ ID NO: 30.

178. (Currently amended) The method of claim 177, wherein the antibody further comprises donor residues at positions 68 and 70 in SEQ ID NO:8 heavy chain variable region is further modified to include one or more backmutations and comprises a framework residue selected from one or more of positions 68 and 70 (linear numbering) occupied by Ala and Leu, respectively.

179. (Currently amended) The method of claim 175, wherein the anti-CD22 antibody comprises a variable domain of the light chain comprising a human acceptor framework region based on SEQ ID NOS:17 and 18 and further comprising donor residues at positions 2, 4, 42, 43, 50 and 65 light chain variable region is further modified to include one or more backmutations and comprises a framework residue selected from one or more of positions 2, 4, 42, 43, 50, and 65 (linear numbering) occupied by Val, Val, Leu, His, Gln, and Asp, respectively, wherein the remainder of the light chain framework region is occupied by residues of the human acceptor framework of SEQ ID NO: 28.

180. (Currently amended) The method of claim 179, wherein the anti-CD22 antibody further comprises a donor residue at position 3 in SEQ ID NO:7 light chain variable region is further modified to include one or more backmutations and comprises a framework residue at position 3 (linear numbering) occupied by Val.

181. (Previously presented) The method of claim 173, wherein the cytotoxic drug is calicheamicin.

182. (Previously presented) The method of claim 181, wherein the calicheamicin is gamma calicheamicin or N-acetyl gamma calicheamicin.

183. (Previously presented) The method of claim 181, wherein the calicheamicin derivative is functionalized with 3-mercapto-3-methyl butanoyl hydrazide.

184. (Previously presented) The method of claim 173, wherein the therapeutically effective dose of the composition is administered subcutaneously, intraperitoneally, intravenously, intraarterially, intramedullarly, intrathecally, transdermally, transcutaneously, intranasally, topically, enterally, intravaginally, sublingually or rectally.

185. (Previously presented) The method of claim 173, wherein the therapeutically effective dose of the composition is administered intravenously.

186. (Previously presented) The method of claim 173, wherein the subject is a human subject.

187. (Previously presented) The method of claim 173, wherein the B-cell malignancy is a leukemia, a lymphoma or a Non-Hodgkin's lymphoma.

188-189. (Canceled)

190. (Previously presented) The method of claim 173, comprising administering the therapeutically effective dose of the composition with one or more bioactive agents.

191. (Previously presented) The method of claim 190, wherein the one or more bioactive agents are antibodies.

192. (Previously presented) The method of claim 191, wherein the antibody is directed against a cell surface antigen expressed on B-cell malignancies.

193. (Previously presented) The method of claim 192, wherein the antibody directed against cell surface antigens expressed on B-cell malignancies is selected from a group consisting of anti-CD19, anti-CD20 and anti-CD33 antibodies.

194. (Previously presented) The method of claim 193, wherein the anti-CD20 antibody is rituximab.

195. (Previously presented) The method of claim 191, wherein the therapeutically effective dose of the composition is administered together with an antibody directed against a cell surface

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antigen on B-cell malignancies, and optionally comprising one or more combinations of cytotoxic agents as a part of a treatment regimen, wherein the combination of cytotoxic agents is selected from:

A. CHOPP (cyclophosphamide, doxorubicin, vincristine, prednisone, and procarbazine);

B. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone);

C. COP (cyclophosphamide, vincristine, and prednisone);

D. CAP-BOP (cyclophosphamide, doxorubicin, procarbazine, bleomycin, vincristine, and prednisone);

E. m-BACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine, dexamethasone, and leucovorin);

F. ProMACE-MOPP (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, mechloethamine, vincristine, prednisone, and procarbazine);

G. ProMACE-CytaBOM (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, cytarabine, bleomycin, and vincristine);

H. MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, fixed dose prednisone, bleomycin, and leucovorin);

I. MOPP (mechloethamine, vincristine, prednisone, and procarbazine);

J. ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

K. MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABV (adriamycin/doxorubicin, bleomycin, and vinblastine);

L. MOPP(mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

M. ChlVPP (chlorambucil, vinblastine, procarbazine, and prednisone);

N. IMVP-16 (ifosfamide, methotrexate, and etoposide);

O. MIME (methyl-gag, ifosfamide, methotrexate, and etoposide);

P. DHAP (dexamethasone, high-dose cytarabine and cisplatin);

Q. ESHAP (etoposide, methylpredisolone, high-dose cytarabine, and cisplatin);

R. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

S. CAMP (lomustine, mitoxantrone, cytarabine, and prednisone);

T. CVP-1 (cyclophosphamide, vincristine, and prednisone). ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

U. ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

V. EPOCH (etoposide, vincristine, and doxorubicin for 96 hours with bolus doses of cyclophosphamide and oral prednisone);

W. ICE (ifosfamide, cyclophosphamide, and etoposide);

X. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

Y. CHOP-B. (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin); and

Z. P/DOCE (epirubicin or doxorubicin, vincristine, cyclophosphamide, and prednisone).

196. (Currently amended) A method of treating a subject with a B-cell malignancy that expresses CD22 antigen, the method comprising administering to the subject a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate, wherein the anti-CD22 antibody of the monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate comprises SEQ ID NO:1 for CDR-H1, SEQ ID NO: 2 or SEQ ID NO:13 or SEQ ID NO:15 or SEQ ID NO:16 or residues 50-66 of SEQ ID NO:27 or residues 50-66 of SEQ ID NO:24 or residues 50-66 of SEQ ID NO:26 for CDR-H2, SEQ ID NO:3 for CDR-H3, SEQ ID NO:4 for CDR-L1, SEQ ID NO:5 for CDR-L2, and SEQ ID NO:6 for CDR-L3.

197. (Previously presented) The method of claim 196, wherein the anti-CD22 antibody is selected from a group consisting of a monoclonal antibody, a chimeric antibody, a human antibody, a humanized antibody, a single chain antibody, and a biologically active antibody fragment wherein the biologically active fragment is a Fab, a modified Fab, Fab', F(ab')2 or Fv, or a heavy chain monomer or dimer.

198. (Previously presented) The method of claim 197, wherein the anti-CD22 antibody is a humanized antibody.

199. (Previously presented) The method of claim 198, wherein the humanized antibody comprises a variable domain comprising human acceptor framework regions and non-human donor CDRs.

200. (Currently amended) The method of claim 199, wherein the human acceptor framework regions of the variable domain of the heavy chain of the antibody are based on SEQ ID NOS:21 and 22 and comprise donor residues at positions 1, 28, 48, 72 and 97 in SEQ ID NO:8 anti-CD22 antibody comprises a heavy chain framework residue selected from one or more of positions 1, 28, 48, 72, and 97 (linear numbering) occupied by Glu, Arg, Ile, Ala, and Thr, respectively, wherein the remainder of the heavy chain framework region is occupied by residues of the human acceptor framework of SEQ ID NO: 21 or 22.

201. (Currently amended) The method of claim 200, wherein the anti-CD22 antibody further comprises donor residues at positions 68 and 70 in SEQ ID NO:8 a heavy chain framework

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residue selected from one or more of positions 68 and 70 (linear numbering) occupied by Ala and Leu, respectively.

202.   (Currently amended) The method of claim 198, wherein the anti-CD22 antibody comprises a variable domain of the light chain comprising a human acceptor framework region based on SEQ ID NOS:17 and 18 and further comprising donor residues at positions 2, 4, 42, 43, 50 and 65 a light chain framework residue selected from one or more of positions 2, 4, 42, 43, 50, and 65 (linear numbering) occupied by Val, Val, Leu, His, Gln, and Asp, respectively, wherein the remainder of the light chain framework region is occupied by residues of the human acceptor framework of SEQ ID NO: 17 or 18.

203.   (Currently amended) The method of claim 202, wherein the anti-CD22 antibody further comprises a donor residue at position 3 in SEQ ID NO:7 a light chain framework residue at position 3 (linear numbering) occupied by Val.

204.   (Previously presented) The method of claim 196, wherein the cytotoxic drug is calicheamicin.

205.   (Previously presented) The method of claim 204, wherein the calicheamicin is gamma calicheamicin or N-acetyl gamma calicheamicin.

206.   (Previously presented) The method of claim 204, wherein the calicheamicin derivative is functionalized with 3-mercapto-3-methyl butanoyl hydrazide.

207.   (Previously presented) The method of claim 196, wherein the therapeutically effective dose of the composition is administered subcutaneously, intraperitoneally, intravenously, intraarterially, intramedullarly, intrathecally, transdermally, transcutaneously, intranasally, topically, enterally, intravaginally, sublingually or rectally.

208.   (Previously presented) The method of claim 196, wherein the therapeutically effective dose of the composition is administered intravenously.

209.   (Previously presented) The method of claim 196, wherein the subject is a human subject.

210. (Previously presented) The method of claim 196, wherein the B-cell malignancy is a leukemia, a lymphoma or a Non-Hodgkin's lymphoma.

211-212. (Canceled)

213. (Previously presented) The method of claim 196, comprising administering the therapeutically effective dose of the composition with one or more bioactive agents.

214. (Previously presented) The method of claim 213, wherein the one or more bioactive agents are antibodies.

215. (Previously presented) The method of claim 214, wherein the antibody is directed against a cell surface antigen expressed on B-cell malignancies.

216. (Previously presented) The method of claim 215, wherein the antibody directed against cell surface antigens expressed on B-cell malignancies is selected from a group consisting of anti-CD19, anti-CD20 and anti-CD33 antibodies.

217. (Previously presented) The method of claim 216, wherein the anti-CD20 antibody is rituximab.

218. (Previously presented) The method of claim 214, wherein the therapeutically effective dose of the composition is administered together with an antibody directed against a cell surface antigen on B-cell malignancies, and optionally comprising one or more combinations of cytotoxic agents as a part of a treatment regimen, wherein the combination of cytotoxic agents is selected from:

    A. CHOPP (cyclophosphamide, doxorubicin, vincristine, prednisone, and procarbazine);

    B. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone);

    C. COP (cyclophosphamide, vincristine, and prednisone);

    D. CAP-BOP (cyclophosphamide, doxorubicin, procarbazine, bleomycin, vincristine, and prednisone);

E. m-BACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine, dexamethasone, and leucovorin);

F. ProMACE-MOPP (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, mechloethamine, vincristine, prednisone, and procarbazine);

G. ProMACE-CytaBOM (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, cytarabine, bleomycin, and vincristine);

H. MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, fixed dose prednisone, bleomycin, and leucovorin);

I. MOPP (mechloethamine, vincristine, prednisone, and procarbazine);

J. ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

K. MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABV (adriamycin/doxorubicin, bleomycin, and vinblastine);

L. MOPP(mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

M. ChlVPP (chlorambucil, vinblastine, procarbazine, and prednisone);

N. IMVP-16 (ifosfamide, methotrexate, and etoposide);

O. MIME (methyl-gag, ifosfamide, methotrexate, and etoposide);

P. DHAP (dexamethasone, high-dose cytarabine and cisplatin);

Q. ESHAP (etoposide, methylpredisolone, high-dose cytarabine, and cisplatin);

R. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

S. CAMP (lomustine, mitoxantrone, cytarabine, and prednisone);

T. CVP-1 (cyclophosphamide, vincristine, and prednisone). ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

U. ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

V. EPOCH (etoposide, vincristine, and doxorubicin for 96 hours with bolus doses of cyclophosphamide and oral prednisone);

W. ICE (ifosfamide, cyclophosphamide, and etoposide);

X. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

Y. CHOP-B. (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin); and

Z. P/DOCE (epirubicin or doxorubicin, vincristine, cyclophosphamide, and prednisone).

219. (Currently amended) A method of treating a subject with a B-cell malignancy that expresses CD22 antigen, the method comprising administering to the subject a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate, wherein the anti-CD22 antibody of the monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate comprises a light chain variable region having a sequence set forth in SEQ ID NO:7 and a heavy chain variable region having a sequence set forth in SEQ ID NO:8.

220. (Previously presented) The method of claim 219, wherein the anti-CD22 antibody is selected from a group consisting of a monoclonal antibody, a chimeric antibody, a human antibody, a humanized antibody, a single chain antibody, and a biologically active antibody fragment wherein the biologically active fragment is a Fab, a modified Fab, Fab', F(ab')2 or Fv, or a heavy chain monomer or dimer.

221. (Previously presented) The method of claim 220, wherein the anti-CD22 antibody is a chimeric antibody.

222. (Previously presented) The monomeric cytotoxic drug derivative/carrier conjugate of claim 220, wherein the humanized antibody comprises a variable domain comprising human acceptor framework regions and non-human donor CDRs.

223-226. (Canceled)

227. (Previously presented) The method of claim 219, wherein the cytotoxic drug is calicheamicin.

228. (Previously presented) The method of claim 227, wherein the calicheamicin is gamma calicheamicin or N-acetyl gamma calicheamicin.

229. (Previously presented) The method of claim 227, wherein the calicheamicin derivative is functionalized with 3-mercapto-3-methyl butanoyl hydrazide.

230. (Previously presented) The method of claim 219, wherein the therapeutically effective dose of the composition is administered subcutaneously, intraperitoneally, intravenously, intraarterially, intramedullarly, intrathecally, transdermally, transcutaneously, intranasally, topically, enterally, intravaginally, sublingually or rectally.

231. (Previously presented) The method of claim 230, wherein the therapeutically effective dose of the composition is administered intravenously.

232. (Previously presented) The method of claim 219, wherein the subject is a human subject.

233. (Previously presented) The method of claim 219, wherein the B-cell malignancy is a leukemia, a lymphoma or a Non-Hodgkin's lymphoma.

234-235. (Canceled)

236. (Previously presented) The method of claim 219, comprising administering the therapeutically effective dose of the composition of the monomeric cytotoxic drug derivative/anti-CD22-antibody conjugate with one or more bioactive agents.

237. (Previously presented) The method of claim 236, wherein the one or more bioactive agents are antibodies.

238. (Previously presented) The method of claim 237, wherein the antibody is directed against a cell surface antigen expressed on B-cell malignancies.

239. (Previously presented) The method of claim 238, wherein the antibody directed against cell surface antigens expressed on B-cell malignancies is selected from a group consisting of anti-CD19, anti-CD20 and anti-CD33 antibodies.

240. (Previously presented) The method of claim 239, wherein the anti-CD20 antibody is rituximab.

241. (Previously presented) The method of claim 237, wherein the therapeutically effective dose of the composition is administered together with an antibody directed against a cell surface antigen on B-cell malignancies, and optionally comprising one or more combinations of cytotoxic agents as a part of a treatment regimen, wherein the combination of cytotoxic agents is selected from:

    A. CHOPP (cyclophosphamide, doxorubicin, vincristine, prednisone, and procarbazine);

    B. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone);

    C. COP (cyclophosphamide, vincristine, and prednisone);

    D. CAP-BOP (cyclophosphamide, doxorubicin, procarbazine, bleomycin, vincristine, and prednisone);

    E. m-BACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine, dexamethasone, and leucovorin);

    F. ProMACE-MOPP (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, mechloethamine, vincristine, prednisone, and procarbazine);

    G. ProMACE-CytaBOM (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, cytarabine, bleomycin, and vincristine);

    H. MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, fixed dose prednisone, bleomycin, and leucovorin);

I.   MOPP (mechloethamine, vincristine, prednisone, and procarbazine);

J.   ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

K.   MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABV (adriamycin/doxorubicin, bleomycin, and vinblastine);

L.   MOPP(mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);

M.   ChlVPP (chlorambucil, vinblastine, procarbazine, and prednisone);

N.   IMVP-16 (ifosfamide, methotrexate, and etoposide);

O.   MIME (methyl-gag, ifosfamide, methotrexate, and etoposide);

P.   DHAP (dexamethasone, high-dose cytarabine and cisplatin);

Q.   ESHAP (etoposide, methylpredisolone, high-dose cytarabine, and cisplatin);

R.   CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

S.   CAMP (lomustine, mitoxantrone, cytarabine, and prednisone);

T.   CVP-1 (cyclophosphamide, vincristine, and prednisone). ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

U.   ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);

V.   EPOCH (etoposide, vincristine, and doxorubicin for 96 hours with bolus doses of cyclophosphamide and oral prednisone);

W.   ICE (ifosfamide, cyclophosphamide, and etoposide);

X.   CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);

Y.   CHOP-B. (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin); and

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Z. P/DOCE (epirubicin or doxorubicin, vincristine, cyclophosphamide, and prednisone).

242. (Currently amended) A method of treating a subject with aggressive lymphomas <u>that</u> <u>expresses CD22 antigen</u> comprising administering to the subject a patient in need of said treatment a therapeutically effective dose of a composition comprising a monomeric calicheamicin derivative-anti-CD22-antibody conjugate together with one or more bioactive agents, wherein the monomeric calicheamicin derivative-anti-CD22 antibody conjugate comprises a calicheamicin derivative functionalized with 3-mercapto-3-methyl butanoyl hydrazide and an anti-CD22 antibody comprising SEQ ID NO:1 for CDR-H1, SEQ ID NO: 2 or SEQ ID NO:13 or SEQ ID NO:15 or SEQ ID NO:16 or residues 50-66 of SEQ ID NO:27 <u>or</u> <u>residues 50-66 of SEQ ID NO:24 or residues 50-66 of SEQ ID NO:26</u> for CDR-H2, SEQ ID NO:3 for CDR-H3, SEQ ID NO:4 for CDR-L1, SEQ ID NO:5 for CDR-L2, and SEQ ID NO:6 for CDR-L3.

243. (Previously presented) The method of claim 242, wherein the anti-CD22 antibody comprises a variable domain comprising human acceptor framework regions and non-human donor CDRs.

244. (Currently amended) The method of claim 243, wherein the ~~human acceptor framework~~ ~~regions of the variable domain of the heavy chain of the antibody are based on SEQ ID NOS:21~~ ~~and 22 and comprise donor residues at positions 1, 28, 48, 72 and 97 in SEQ ID NO:8~~ <u>anti-CD22</u> <u>antibody comprises a heavy chain framework residue selected from one or more of positions 1,</u> <u>28, 48, 72, and 97 (linear numbering) occupied by Glu, Arg, Ile, Ala, and Thr, respectively,</u> <u>wherein the remainder of the heavy chain framework region is occupied by residues of the</u> <u>human acceptor framework of SEQ ID NO: 21 or 22.</u>

245. (Currently amended) The method of claim 244, wherein the <u>anti-CD22</u> antibody further comprises ~~donor residues at positions 68 and 70 in SEQ ID NO:8~~ <u>a heavy chain framework</u> <u>residue selected from one or more of positions 68 and 70 (linear numbering) occupied by Ala</u> <u>and Leu, respectively.</u>

246. (Currently amended) The method of claim 242, wherein the anti-CD22 antibody comprises ~~a variable domain of the light chain comprising a human acceptor framework region~~

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~~based on SEQ ID NOS:17 and 18 and further comprising donor residues at positions 2, 4, 42, 43,~~ ~~50 and 65~~ <u>a light chain framework residue selected from one or more of positions 2, 4, 42, 43, 50, and 65 (linear numbering) occupied by Val, Val, Leu, His, Gln, and Asp, respectively, wherein the remainder of the light chain framework region is occupied by residues of the human acceptor framework of SEQ ID NO: 17 or 18.</u>

247. (Currently amended) The method of claim 246, wherein the anti-CD22 antibody further comprises ~~a donor residue at position 3 in SEQ ID NO:7~~ <u>a light chain framework residue at position 3 (linear numbering) occupied by Val.</u> .

248. (Previously presented) The method of claim 242, wherein the one or more bioactive agents are antibodies.

249. (Previously presented) The method of claim 248, wherein the antibody is directed against a cell surface antigen expressed on B-cell malignancies.

250. (Previously presented) The method of claim 249, wherein the antibody directed against cell surface antigens expressed on B-cell malignancies is selected from a group consisting of anti-CD19, anti-CD20 and anti-CD33 antibodies.

251. (Previously presented) The method of claim 250, wherein the anti-CD20 antibody is rituximab.

252-256. (Canceled)

257. (New) The method of claim 196, wherein the antibody further comprises a CDR-H2 sequence comprising an amino acid residue at Kabat position 55 other than asparagine.

258. (New) The monomeric cytotoxic drug derivative/carrier conjugate of claim 257, wherein the amino acid residue at Kabat position 55 is glutamine.

259. (New) The monomeric cytotoxic drug derivative/carrier conjugate of claim 196, wherein the antibody comprises a sequence of CDR-H2 comprising an amino acid residue at Kabat position 57 other than threonine.

260.   (New) The monomeric cytotoxic drug derivative/carrier conjugate of claim 259, wherein the amino acid residue at Kabat position 57 is alanine or valine.

261.   (New) The monomeric cytotoxic drug derivative/carrier conjugate of claim 196, wherein the antibody comprises a sequence of CDR-H2 comprising an amino acid residue at Kabat position 60 other than lysine.

262.   (New) The monomeric cytotoxic drug derivative/carrier conjugate of claim 261, wherein the amino acid residue at Kabat position 60 is arginine.

263.   (New) The method of claim 242, wherein the antibody further comprises a CDR-H2 sequence comprising an amino acid residue at Kabat position 55 other than asparagine.

264.   (New) The monomeric cytotoxic drug derivative/carrier conjugate of claim 263, wherein the amino acid residue at Kabat position 55 is glutamine.

265.   (New) The monomeric cytotoxic drug derivative/carrier conjugate of claim 242, wherein the antibody comprises a sequence of CDR-H2 comprising an amino acid residue at Kabat position 57 other than threonine.

266.   (New) The monomeric cytotoxic drug derivative/carrier conjugate of claim 265, wherein the amino acid residue at Kabat position 57 is alanine or valine.

267.   (New) The monomeric cytotoxic drug derivative/carrier conjugate of claim 242, wherein the antibody comprises a sequence of CDR-H2 comprising an amino acid residue at Kabat position 60 other than lysine.

268.   (New) The monomeric cytotoxic drug derivative/carrier conjugate of claim 267, wherein the amino acid residue at Kabat position 60 is arginine.